

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule having at least 80% sequence identity to (a) a nucleic acid molecule that encodes an Mrg polypeptide comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 16, 18, 21, 23, 25, 27, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107 or 109, or (b) the complement of the nucleic acid molecule of (a).

2. An isolated nucleic acid molecule having at least 80% sequence identity to (a) a nucleic acid molecule that encodes a drg-12 polypeptide comprising the amino acid sequence of SEQ ID NO: 14, 19 or 29, or (b) the complement of the nucleic acid molecule of (a).

3. An isolated nucleic acid molecule that hybridizes under stringent conditions to (a) a nucleic acid molecule that encodes an Mrg polypeptide comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 16, 18, 21, 23, 25, 27, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107 or 109, or (b) the complement of the nucleic acid molecule of (a).

4. An isolated nucleic acid molecule that hybridizes under stringent conditions to (a) a nucleic acid molecule that encodes a drg-12 polypeptide comprising the amino acid sequence of SEQ ID NO: 14, 19 or 29, or (b) the complement of the nucleic acid molecule of (a).

5. The isolated nucleic acid molecule of any one of claims 1 to 4 operably linked to an expression control element.

6. The isolated nucleic acid molecule of claim 5 operably linked to a promoter element.

7. A vector comprising the isolated nucleic acid molecule of any one of claims 1 or 2.

8. A host cell comprising the vector of claim 7.

9. The host cell of claim 8, wherein said cell is a prokaryotic cell.

10. The host cell of claim 8, wherein said cell is a eukaryotic cell.

11. The host cell of claim 9, wherein said cell is an *E. coli*.

12. The host cell of claim 10, wherein said cell is a hamster embryonic kidney (HEK) cell.

13. The host cell of claim 10, wherein said cell is a yeast cell.

14. A method for producing a polypeptide comprising culturing the host cell
5 of claim 8 under conditions in which the protein encoded by said nucleic acid is expressed.

15. An isolated polypeptide produced by the method of claim 14.

16. An isolated Mrg polypeptide comprising an amino acid sequence
10 comprising at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 16, 18, 21, 23, 25, 27, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107 or 109.

17. An isolated drg-12 polypeptide comprising an amino acid sequence
15 comprising at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 14, 19 or 29.

18. A chimeric molecule comprising an Mrg polypeptide fused to a heterologous amino acid sequence.

19. The chimeric molecule of claim 18 wherein said heterologous amino acid sequence is an epitope tag sequence.

20. The chimeric molecule of claim 18 wherein said heterologous amino acid sequence is an immunoglobulin constant domain sequence.

21. A chimeric molecule comprising a drg-12 polypeptide fused to a heterologous amino acid sequence.

22. The chimeric molecule of claim 21 wherein said heterologous amino acid
25 sequence is an epitope tag sequence.

23. The chimeric molecule of claim 21 wherein said heterologous amino acid sequence is an immunoglobulin constant domain sequence.

24. An isolated polypeptide exhibiting at least about 40% sequence identity with at least one Mrg polypeptide selected from the group consisting of polypeptides
30 comprising the amino acid sequences of SEQ ID NO: 2, 4, 6, 8, 10, 12, 16, 18, 21, 23, 25, 27, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71,

73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107 and 109, and exhibiting a qualitative biological activity of a native Mrg polypeptide.

25. An isolated polypeptide exhibiting at least about 35% amino acid sequence identity with at least one drg-12 polypeptide selected from the group consisting of polypeptides comprising the amino acid sequences of SEQ ID NO: 14, 19 and 29, and exhibiting a qualitative biological activity of a native drg-12 polypeptide.

26. An isolated antibody that specifically binds to an isolated Mrg polypeptide of claim 16.

27. The isolated antibody of claim 26 wherein said antibody is a monoclonal antibody.

28. The isolated antibody of claim 26 wherein said antibody is an antibody fragment.

29. The isolated antibody of claim 26 wherein said antibody is a humanized antibody.

30. The isolated antibody of claim 26 wherein said antibody is an agonist antibody.

31. The isolated antibody of claim 26 wherein said antibody is a neutralizing antibody.

32. An isolated antibody that specifically binds to an isolated drg-12 polypeptide of claim 17.

33. The isolated antibody of claim 32 wherein said antibody is a monoclonal antibody.

34. The isolated antibody of claim 32 wherein said antibody is an antibody fragment.

35. The isolated antibody of claim 32 wherein said antibody is a humanized antibody.

36. The isolated antibody of claim 32 wherein said antibody is an agonist antibody.

37. The isolated antibody of claim 32 wherein said antibody is a neutralizing antibody.

38. A composition of matter comprising (a) an Mrg polypeptide, (b) a drg-12 polypeptide, (c) an anti-Mrg antibody, or (d) an anti-drg-12 antibody in admixture with a pharmaceutically acceptable carrier.

39. An article of manufacture comprising:

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a container;

a composition of matter of claim 38; and

instructions for using the composition of matter to treat impaired sensory perception in a mammal.

40. A method of identifying Mrg expression in a sample comprising
10 contacting said sample with an anti-Mrg antibody and determining binding of said antibody to the sample.

41. The method of claim 40 wherein said sample is obtained from a patient experiencing impaired sensory perception.

42. The method of claim 41 wherein said patient is experiencing pain.

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43. A method of identifying a compound that binds to an Mrg polypeptide comprising the steps of:

1) contacting a test compound with at least a portion of an Mrg polypeptide; and

2) detecting Mrg/test compound complexes.

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44. The method of claim 43 wherein at least one of the test compound or the Mrg polypeptide is attached to a solid support.

45. The method of claim 44 wherein said solid support is a microtiter plate.

46. The method of claim 43 wherein said Mrg polypeptide is present in a cell membrane.

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47. The method of claim 46 wherein said Mrg polypeptide is present in a fraction of cell membrane prepared from cells expressing an Mrg polypeptide.

48. The method of claim 43 wherein said Mrg polypeptide is present in an immunoadhesin.

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49. The method of claim 43 wherein said test compound is selected from the group consisting of peptides, peptide mimetics, antibodies, small organic molecules and small inorganic molecules.

50. The method of claim 49 wherein said test compound is a peptide.
51. The method of claim 50 wherein said peptide is anchored to a solid support by specifically binding an immobilized antibody.
52. The method of claim 43 wherein said Mrg polypeptide is labeled.
- 5 53. The method of claim 43 wherein said test compound is labeled.
54. The method of claim 43 wherein said test compound is contained in a cellular extract.
55. The method of claim 54 wherein said cellular extract is prepared from cells known to express an Mrg polypeptide.
- 10 56. The method of claim 55 wherein said cellular extract is prepared from dorsal root ganglion cells.
57. A method of identifying a molecule that binds to an Mrg polypeptide comprising the steps of:
 - 1) contacting a host cell expressing an Mrg polypeptide with a test
15 compound; and
 - 2) determining binding of said test compound to said host cell.
58. The method of claim 57 wherein said test compound is labeled.
59. The method of claim 58 wherein said test compound is radioactively
labelled.
- 20 60. The method of claim 57 wherein said host cell is a eukaryotic cell.
61. The method of claim 60 wherein said host cell is a COS cell.
62. A method of identifying a compound that binds an Mrg polypeptide comprising the steps of:
 - 1) contacting an Mrg polypeptide or fragment thereof with a test
25 compound and a known ligand under conditions where binding can occur; and
 - 2) determining the ability of the test compound to interfere with binding of the known ligand.
63. The method of claim 62 wherein said Mrg polypeptide is contacted with the known ligand prior to being contacted with the test compound.
- 30 64. The method of claim 62 wherein said known ligand is an RFamide peptide.

65. A method for identifying a compound that modulates expression of a nucleic acid encoding an Mrg receptor comprising the steps of:

1) exposing a host cell, transformed with a nucleic acid encoding a chimeric polypeptide comprising an Mrg polypeptide and a reporter protein, to a test compound; and

2) determining if there is differential expression of the reporter gene in cells exposed to the test compound compared to control cells that were not exposed to the test compound.

66. A method for identifying an Mrg polypeptide agonist comprising the steps of:

1) contacting a host cell known to be capable of producing a second messenger responses and expressing an Mrg polypeptide with a potential agonist; and

2) measuring a second messenger response.

67. The method of claim 66 wherein said host cell is a eukaryotic cell.

68. The method of claim 67 wherein said host cell is a hamster embryonic kidney (HEK) cell.

69. The method of claim 68 wherein said HEK cell expresses $G\alpha_{15}$.

70. The method of claim 66 wherein measuring a second messenger response comprises measuring a change in intercellular calcium concentration.

71. The method of claim 70 wherein said change in intercellular calcium concentration is measured with FURA-2 calcium indicator dye.

72. The method of claim 66 wherein measuring a second messenger response comprises measuring the flow of current across the membrane of the cell.

73. The method of claim 66 wherein the identified agonist is useful in treating impaired sensory perception in a mammal.

74. The method of claim 73 wherein said impaired sensory perception is pain.

75. A method for identifying an Mrg polypeptide antagonist comprising the steps of:

1) contacting a host cell known to be capable of producing a second messenger response and expressing an Mrg polypeptide with a known Mrg polypeptide agonist and a candidate antagonist;

2) measuring a second messenger response.

5 76. The method of claim 75 wherein said host cell is a eukaryotic cell.

77. The method of claim 76 wherein said host cell is a hamster embryonic kidney (HEK) cell.

78. The method of claim 75 wherein said known Mrg polypeptide agonist is an RFamide peptide.

10 79. The method of claim 75 wherein said second messenger response is a change in intercellular calcium concentration.

80. The method of claim 75 wherein said second messenger response is a change in the flow of current across the membrane of the cell.

15 81. The method of claim 75 wherein the identified antagonist is useful in treating impaired sensory perception in a mammal.

82. A method of identifying an Mrg polypeptide agonist antibody comprising the steps of:

1) preparing a candidate agonist antibody that specifically binds to an Mrg polypeptide;

20 2) contacting a host cell known to be capable of producing a second messenger response and expressing said Mrg polypeptide with the candidate agonist antibody; and

3) measuring a second messenger response.

25 83. A method of identifying an Mrg polypeptide neutralizing antibody comprising the steps of:

1) preparing a candidate neutralizing antibody that specifically binds an Mrg polypeptide;

30 2) contacting a host cell known to be capable of producing a second messenger response and expressing said Mrg polypeptide with the candidate neutralizing antibody; and

3) measuring a second messenger response.

5 84. A transgenic non-human mammal with increased or decreased expression levels of an Mrg polypeptide, wherein said transgenic mammal has stably integrated into its genome a nucleic acid molecule encoding an Mrg polypeptide of claim 16.

 85. A method of treating impaired sensory perception in a mammal comprising administering to said mammal an agent that increases the expression of a polypeptide of claim 16 in said mammal.

10 86. The method of claim 85 wherein said impaired sensory perception is pain.